Relationship between seasonal serum 25-hydroxyvitamin d levels and disease activity in patients with ankylosing spondylitis, osteoarthritis and fibromyalgia syndrome

Ankilozan spondilit, osteoartrit, fibromiyalji sendromu hastalarında mevsimsel serum 25 hidroksi vitamin d düzeyleri ile hastalık aktivitesi arasındaki ilişki

Vitamin d levels in ankylosing spondylitis, osteoarthritis, fibromyalgia

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Öz

Amaç: Bu çalışmada ankilozan spondilit (AS), osteoartrit (OA), fibromiyalji sendromu (FMS) tanılı hastalarda ve sağlıklı kontrollerde mevsimsel D vitamini düzeyleri ile hastalık aktivitesi arasındaki ilişkiyi araştırmayı amaçladık. Gereç ve Yöntem: Çalışmaya AS tanılı 32, OA tanılı 25, FMS tanılı 25 hasta ve 25 sağlıklı kontrol dahil edildi. Mevsimsel 25(OH) vitamin D yazın Temmuz, Ağustos ve Eylül aylarında kışın aralık, ocak ve şubat aylarında ölçüldü. Hastalık aktiviteleri AS hastalarında Bath Ankilozan Spondilit Hastalık Aktivite Indeksi (BASDAI), OA hastalarında Western Ontarıo ve McMaster Universitesi Osteoartrit Indeksi (WOMAC) ve FMS hastalarında fibromiyalji etki anketi (FIQ) ile hastane anksiyete depresyon skalası (HAD) kullanılarak hesaplandı. Bulgular: Çalışmamızda AS hastalarında yaz BASDAI değeri ile kış BASDAI değeri arasında istatistiksel olarak anlamlı farklılık yoktu ($p>0.05$) ve vitamin D düzeyleri ile BASDAI değerleri arasında ilişki kurulamadı. OA grubunda yaz WOMAC ortalama değeri ile kış WOMAC ortalama değeri arasında anlamlı farklılık saptandı ($p<0.05$) ve vitamin D düzeyleri kışın anlamlı olarak düşüktü. WOMAC değerleri ile vitamin D düzeyleri arasında negatif yönde anlamlı ilişki bulundu. FMS hastalarında ise FIQ değerleri ile mevsimsel D vitamini arasında negatif anlamlı değişim varken HAD skoru ile mevsimsel D vitamin düzeyleri arasında ilişki kurulamadı. Tartışma: Özellikle OA ve FMS hastalarında hastalık aktivitesinin düzenlenmesine katkıda bulunması açısından D vitamini düzeylerinin belirlenmesi ve gerekli hastalarda suplementasyonun yapılması önemlidir.

Anahtar Kelimeler

Ankilozan Spondilit; Osteoartrit; Fibromiyalji Sendromu; Hastalık Aktivitesi; Vitamin D

Abstract

Aim: In this study, we aimed to investigate the relationship between seasonal vitamin D levels and disease activity in patients with ankylosing spondylitis (AS), osteoarthritis (OA), fibromyalgia syndrome (FMS) and healthy controls. Material and Method: The study included 32 patients with AS, 25 patients with OA, 25 patients with FMS and 25 healthy controls. Bi-seasonal measurements of serum vitamin D were checked in July, August, and September for summertime and in December, January and February for wintertime. Disease activity was evaluated by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Fibromyalgia Impact Questionnaire (FIQ)-Hospital Anxiety and Depression Scale (HAD) in groups of AS, OA, and FMS patients respectively. Results: In our study, there was no statistically significant difference between summer BASDAI values and winter BASDAI values in patients with AS ($p> 0.05$), and there was no relationship between vitamin D levels and BASDAI values. There was a statistically significant difference between summer WOMAC mean value and winter WOMAC mean value in OA group ($p<0.05$) and vitamin D levels were significantly lower in winter. There was a significant negative correlation between WOMAC values and vitamin D levels. In patients with FMS, there was a negative significant difference between FIQ values and seasonal vitamin D, but this relationship was not found between HAD score and seasonal vitamin D levels. Discussion: Especially in patients with OA and FMS, it is important to determine vitamin D levels and to provide supplementation to patients in terms of contributing to the regulation of disease activity.

Keywords

Ankylosing Spondylitis; Osteoarthritis; Fibromyalgia Syndrome; Disease Activity; Vitamin D

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Introduction

Vitamin D is a steroid hormone which is involved in calcium and phosphorus metabolism and thus plays a role in bone formation and resorption. It modulates gene expression by acting at the cell level [1]. In addition to its metabolic effects, it plays an important role in the regulation of the immune system [2]. It suppresses the production of cytokines such as IL-1, IL-6, IL-12, and TNF-alpha produced in macrophages and also blocks antigen presentation [3,4]. In genetic and epidemiological studies, vitamin D has been shown to play a potential role, particularly in the pathogenesis and prevention of autoimmune diseases such as type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus [5]. It has been reported that 70% of the patients who presented to a rheumatology outpatient clinic had vitamin D deficiency, and 26% had severe deficiency [6].

Ankylosing spondylitis (AS) is an inflammatory disease of unknown etiology that characterized by involvement of the spine, sacroiliac joint, and peripheral joint. It begins in the second or third decade of life, and the ratio of female to male is 3/1 [7]. It begins with inflammation of the tendon, ligament, and joint capsule attachment sites and, further on, results in fusion of the entire spinal cord. In addition, osteoporosis is a comorbid disease that often accompanies early stages of the disease. Vitamin D deficiency can trigger osteoporosis in these patients. In addition, the relationship between disease activity and vitamin D has recently been the subject of many studies. Some studies demonstrated that low vitamin D levels are associated with high disease activity [8,9]. Conversely, there are also studies which did not identify any association between disease activity and vitamin D levels [10,11].

Osteoarthritis (OA) is a degenerative and progressive joint disease. OA starts with synovial inflammation in the early period and continues with loss of cartilage, abnormal subchondral bone growth, and remodeling. As is known, vitamin D plays a role in normal bone and cartilage metabolism. Vitamin D is thought to be an effective factor in the pathogenesis of OA and disease progression and has been supported by various studies. Vitamin D deficiency has been shown in 24% of patients with advanced stage OA [12]. In a study that evaluated patients younger than 60 years, a positive relationship was found between low D vitamin levels and knee OA, and a stronger association was also shown in younger patients [13]. However, in contrast to these data, a study on non-OA patients showed that low vitamin D levels were not associated with the risk of developing knee or hip OA after a 10-year follow-up [14].

Fibromyalgia syndrome (FMS) is a rheumatic disease characterized by chronic pain, fatigue, physical and/or psychological symptoms [15]. Its incidence in general population ranges from 2.9% to 3.8%, with the majority being women [16,17]. Although pain is the major symptom, it's usually accompanied by symptoms such as fatigue, sleep problems, cognitive dysfunction, dysesthesia, anxiety, depression, and headache. FMS is the prototype of chronic pain syndromes. The association between chronic pain and vitamin D deficiency is based on limited clinical evidence. Vitamin D is known to be effective in pathogenesis, and pathways associated with cortical, immunological, hormonal, and neuronal changes are thought to be potentially affected by vitamin D levels [18]. In a study by Wepner et al. [19], when replacement therapy was administered to patients diagnosed with FMS having vitamin D deficiency, significant improvements were noted in pain, quality of life, and emotional state questionnaires of these patients. However, in contrast to these findings, in a systematic review, it was reported that there was no difference between serum vitamin D levels of healthy people and FMS patients [20].

The aim of this study was to investigate the relationship between seasonal vitamin D levels and disease activity in AS, OA and FMS patients and to show the importance of vitamin D replacement in these patients.

Material and Method

Participants

Among patients who presented to our outpatient clinic, 40 AS patients who met the Modified Newyork criteria, 40 OA patients who were diagnosed according to American College of Rheumatology (ACR) criteria, 40 patients clinically diagnosed with FMS according to 2010 ACR criteria and 40 healthy controls were included in this prospective controlled study. Patients aged 65 and older, patients with active liver disease or cirrhosis, patients with renal insufficiency and active renal disease, those with a history of malignancy, previous hip or knee operation, pregnant women, those with thyroid or parathyroid diseases that impair bone metabolism, and patients who used vitamin D and calcium derivatives for replacement in the last 3 months were excluded from the study.

All participants were informed about the study and their consent in verbal and written form was obtained. Our study was approved by the hospital ethics committee (Approval no: 191). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Assessments

All participants' demographic information (age, sex, education level), body mass index (BMI), calcium intake with food, smoking, sunbathing, laboratory tests (calcium, phosphorus, parathormone, C-reactive protein, sedimentation, vitamin D), pain level with visual analogue scale (VAS), fatigue scale, patient global assessment of disease and physician global assessment of disease were recorded. Seasonal 25 (OH) vitamin D was measured by high-pressure liquid chromatography (HPLC) method in winter in December, January, February and in summer in July, August and September.

Disease activity was evaluated by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Fibromyalgia Impact Questionnaire (FIQ)-Hospital Anxiety and Depression Scale (HAD) in groups of AS, OA, and FMS patients respectively.

Visual Analogue Scale (VAS): All patients were asked to evaluate their pain using 10 cm VAS. In addition, the fatigue scale, in which the physician and the patient evaluate pain, fatigue and disease activity, the scale of patient global assessment of disease and the scale of physician global assessment of disease were completed.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): It

was developed to determine disease activity in AS patients. A 10-cm visual analog scale is used. It consists of a total of 6 questions pertaining to 5 major symptoms in AS patients, which includes 2 questions about morning stiffness. The BASDAI score increases with increasing disease activity [21].

Western Ontario and McMaster University Osteoarthritis Index (WOMAC): It evaluates pain, stiffness, and physical functioning in OA of the knee. It consists of 24 questions and the patient's condition in the last 48 hours is recorded on a scale of 0-4 points. In WOMAC index, 0=no pain/no limitation, 1=mild pain/limitation, 2=moderate pain/limitation, 3=severe pain/limitation, 4=very severe pain/limitation. High scores indicate severe OA [22].

Fibromyalgia Impact Questionnaire (FIQ): A specific measure of physical function and health status in FMS. It was developed by Burckhardt et al. [23] in 1991 and reorganized by Bennett [24] in 2005. FIQ consists of 10 items. In the inquiry, the first item contains a scale on which 11 daily activities are evaluated over 0-3. The second item questions the number of days the patient felt well during the past week, while the third questions the number of days the patient was unable to go to work or do housework due to illness during the past week. The other seven evaluates the severity of pain, ability to do job, fatigue, resting state after sleep, stiffness, anxiety, and depression during the past week using VAS. The total FIQ score is a maximum of 100 points. High scores indicate low functionality level [23].

Hospital Anxiety and Depression Scale (HAD): An assessment tool developed to identify the risk of anxiety and depression and measure its level and change of severity. Its subscales are anxiety (HAD-A) and depression (HAD-D). It contains 14 questions in total, including 7 (odd numbers) measuring anxiety and 7 (even numbers) measuring depression. The cut-off point was found to be 10/11 for anxiety subscale and 7/8 for depression subscale. According to this, those scoring higher than these points are assessed as a risk group. The lowest and highest scores that a person can get from either subscale are 0 and 21, respectively [25].

Statistical Analysis

SPSS Statistics Version 16 software package was used in statistical analysis of the data. Pearson Chi-Square and Fisher's Exact test were used to compare categorical data between the groups; continuous variables did not fit normal distribution (Kolmogorov Smirnov and Shapiro-Wilk p<0.05) so Kruskal Wallis H (Mann Whitney U with post hoc Bonferroni correction) was used to compare the data between more than two groups, and Wilcoxon Signed Ranks statistical analysis was used to compare summer values with winter values. Correlations of variables were evaluated by Pearson correlation analysis. P<0.05 was considered statistically significant.

Results

A total of 160 participants from each group, including 40 volunteers, were included in the study. 53 participants, including 8 from the AS group, 15 from the OA group, 15 from the FMS group and 15 from the control group, did not come to second follow-up, so a total of 107 participants were assessed. Of the 107 participants, 32 were from the AS, 25 from the OA, 25 from the FMS and 25 from the control groups. Significant differences were found between the groups by age (p <0.001), sex (p = 0.001) and BMI (p = 0.004). The highest mean age was in the OA group, and the lowest mean age was in the AS group. A statistically significant difference was found between the groups when the distribution of educational level in the groups was examined (p=0.001). Educational level was high in the control group and low in other groups. The highest number of osteoporosis patients was in the OA group, whereas there were no patients with osteoporosis in the FMS group and a significant difference was present (p=0.014). There was no significant difference between the groups by sunbathing rates, dietary habits, tobacco use, and calcium intake with food (p> 0.05). Some demographic and clinical characteristics of the groups are shown in Table 1.

Table 1. Demographic and clinical characteristics of the groups

	AS (n=32)	OA (n=25)	FMS (n=25)	CNT (n=25)	p
Age (years)	38.59±8.62	56.92±4.73	46.12±7.46	44.52±13.96	<0.001
Sex (F/M), n	5/27	23/2	24/1	18/7	0.001
BMI (kg/m^2)	27.52±3.81	29.75±3.96	30.92±4.43	31.77±4.64	0.004
Sunbathing rates, n %					0.757
Never	12 (37.5)	12 (48)	15 (60)	14 (56)	
One month	14 (43.8)	8 (32)	6 (24)	8 (32)	
Two months	2 (6.3)	2 (8)	2 (8)	0 (0)	
Three months	4 (12.5)	3 (12)	2 (8)	3 (12)	
Osteoporosis, n %					0.014
Present	4 (12.5)	7 (28.0)	0 (0)	6 (24.0)	
None	28 (87.5)	18 (72.0)	25 (100)	19 (76.0)	

Data mean±standard deviation or n (%)
AS: Ankylosing Spondylitis, BMI: Body Mass Index, CNT: Control, F: Female, FMS: Fibromyalgia Syndrome, M: Male, OA: Osteoarthritis

There was no significant difference between the groups by calcium, phosphorus, parathormone (PTH), C reactive protein (CRP), sedimentation (ESR) and mean summer and winter vitamin D levels (p> 0.05). However, in intra-group assessments, summer and winter vitamin D levels showed statistically significant differences in all groups (p=0.001). The highest and lowest summer vitamin D levels were found in the control group and the OA group, respectively. The highest winter vitamin D level was found in the control group too, while the lowest winter vitamin D level was measured in the AS group. The laboratory values of the groups are summarized in Table 2.

Patient global assessment, VAS and fatigue summer and winter values showed statistically significant differences between the groups (p<0.001). In the intragroup evaluations, there was no significant difference between summer and winter VAS, patient global assessment and fatigue levels in the AS group, whereas summer and winter levels were different in OA, FMS and control groups (p = 0.001). Summer and winter values of physician global assessment score were significantly different between the groups (p<0.001). In the intragroup evaluations, there was

Table 2. Comparison of the laboratory values of the groups

	AS (n=32)	OA (n=25)	FMS (n=25)	CNT (n=25)	p
Calcium (mg/dL)	9.39±0.51	9.19±0.47	9.04±0.67	9.12±0.78	0.147
Phosphorus (mg/dL)	3.5±0.63	3.62±0.63	3.5±0.58	3.54±0.81	0.841
PTH (pg/mL)	48.1±16.88	43.3±15.72	52.28±19.3	54.52±18.74	0.147
CRP (mg/dL)	1.19±2.37	0.62±0.61	0.67±1.01	0.62±1.09	0.062
ESR (mm/hour)	17.34±15.48	20.24±13.65	18.68±11.69	20±13.43	0.529
Vitamin D (summer/ winter) (µg/L)	24.38±10.54/ 12.04±7.23 p=0.001[c]	19.23±7.25/ 13.53±8.19 p=0.001[c]	23.46±15.44/ 12.38±7.09 p=0.001[c]	25.88±10.2/ 17.54±11.04 p=0.001[c]	0.102[a] 0.115[b]

Data mean±standard deviation
AS: Ankylosing spondylitis, CNT:Control, CRP:C-reactive protein, ESR: sedimentation, FMS: Fibromyalgia syndrome, OA:Osteoartritis, PTH: parathormone
[a]Intergroup comparison of vitamin D summer values, [b]Intergroup comparison of vitamin D winter values, [c]Intragroup comparison of summer-winter vitamin D values

no significant difference between summer and winter values in the AS group, while a significant difference was identified in the OA, FMS and control groups (p = 0.001). A comparison of some clinical assessment scales of the groups is shown in Table 3. There was no statistically significant difference between summer BASDAI value and winter BASDAI value in the AS group (p> 0.05). There was no correlation between vitamin D levels and BASDAI values. In the OA group, there was a statistically significant difference between summer WOMAC mean value and winter WOMAC mean value (p = 0.003), and vitamin D levels were significantly lower in winter. These results showed a significant negative correlation between WOMAC values and vitamin D levels. In the FMS group, summer FIQ value was significantly lower than winter FIQ value (p = 0.001). However, no significant difference was found between summer and winter HAD values. In conclusion, there was a negative significant change between FIQ values and seasonal vitamin D. However, no correlation was found between HAD score and seasonal vitamin D levels. Summer and winter BASDAI, WOMAC, FIQ values of the groups are shown in Table 4.

Table 3. Comparison of clinical characteristics of the groups

	AS (n=32)	OA (n=25)	FMS (n=25)	CNT (n=25)	p
VAS (summer/ winter)	4.14±2.84/ 3.64±2.81 P=0.410[c]	5.68±1.35/ 6.48±1.36 P=0.001[c]	5.84±2.06/ 7.36±1.75 P=0.001[c]	2.36±1.8/ 3.36±1.89 P=0.001[c]	<0.001[a] <0.001[b]
Patient global assessment (summer/ winter)	4.7±3.17/ 4.16±2.67 P=0.411[c]	5.68±1.35/ 6.52±1.36 P=0.001[c]	6±1.98/ 7.56±1.45 P=0.001[c]	2.28±1.72/ 3.36±1.89 P=0.001[c]	<0.001[a] <0.001[b]
Physician global assessment (summer/ winter)	4.05±2.2/ 3.75±2.45 P=0.600[c]	5.68±1.35/ 6.48±1.36 P=0.001[c]	5.68±1.49/ 7.2±1 P=0.001[c]	2.36±1.7/ 3.44±1.89 P=0.001[c]	<0.001[a] <0.001[b]
Fatigue (summer/ winter)	4.7±3.17/ 4.16±2.67 P=0.411[c]	5.68±1.35/ 6.64±1.38 P=0.001[c]	6.6±1.8/ 8.2±1.22 P=0.001[c]	2.76±2.18/ 3.84±2.15 P=0.001[c]	<0.001[a] <0.001[b]

Data mean±standard deviation
AS: Ankylosing spondylitis, CNT: Control, FMS: Fibromyalgia syndrome, OA: Osteoa rtritis [a]Intergroup comparison of summer values, [b]Intergroup comparison of winter values, [c]Intragroup comparison of summer-winter values

Discussion

In our study, mean BASDAI value in the AS group did not show any significant difference between summer and winter, and there was no correlation between vitamin D and BASDAI in both seasons. In the OA group, WOMAC total score was higher in winter, the change in summer and winter was significant, and a negative correlation was found between vitamin D and WOMAC total score in both seasons. In FMS group, FIQ total score was higher in winter, the change in summer and winter was significant, however, HAD scale value did not show any significant difference in summer and winter. A negative correlation was established between FIQ scores and vitamin D, whereas there was no correlation between HAD scores and vitamin D.

Vitamin D deficiency is a growing problem worldwide. Numerous studies suggested that considering the factors that may lead to vitamin D deficiency, the main reason for the increase in the prevalence of vitamin D deficiency is the decrease in exposure to UV-B radiation, the primary source, and thus sun exposure [26]. It was identified that the decrease in sun exposure arises from traditional clothing worn mostly to protect against harmful effects of the sun in Asia and sunscreens with high UV-protection used in Europe and Americas to protect against skin cancer [27]. In recent years, it has been thought that there is a relationship between autoimmune diseases and vitamin D deficiency, and studies have shifted to this direction. In a study of 384 patients with autoimmune disease conducted by Zheng et al. [28], 57% of patients had vitamin D deficiency, and 33% had vitamin D insufficiency. Skabby et al. [29] stated that high vitamin D levels are protective against autoimmune diseases.

The role of vitamin D in the pathogenesis of AS and disease activity is still unclear. It is thought that the disease is more active in patients with low vitamin D levels. One of the theories is that high anti-TNF levels in active patients suppress 25-hydroxylase enzyme in the kidney [30], whereas according to another theory, these patients have a vitamin D receptor deficiency in their intestines [8]. Urruticoechea-Arana et al. [31] detected vitamin D deficiency in 37% of patients with AS, while Zhang et al. [32] demonstrated severe vitamin D deficiency in AS patients compared to healthy controls. In our study, summer and winter vitamin D levels of AS patients did not show any significant difference compared to the control group. There was also no correlation between seasonal vitamin D levels and BASDAI values. This result is in good agreement with Yazmalar et

Table 4. Comparison of summer and winter BASDAI, WOMAC, FIQ values of the groups.

Group			p
AS	Summer BASDAI	3.98±2.37	0.270
	Winter BASDAI	3.51±2.24	
OA	Summer WOMAC	41.2±16.6	0.003
	Winter WOMAC	49.76±19.5	
FMS	Summer FIQ	58.16±18.28	0.001
	Winter FIQ	76.72±14.7	

Data mean±standard deviation
AS: Ankylosing Spondylitis, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, FIQ: Fibromyalgia Impact Questionnaire, FMS: Fibromyalgia Syndrome, OA: Osteoarthritis

al. [33], who did not identify any significant negative correlation between seasonal vitamin D levels and BASDAI, whereas Erten et al. [34] showed a significant correlation between seasonal variation of vitamin D and CRP and ESR levels, however, they did not identify any significant difference with BASDAI values. Contrary to this data, Hmamouchi et al. [35] found a significant negative correlation between vitamin D and BASDAI. In another study by the same researchers, it was emphasized that radiological sacroiliitis, ASDAS-CRP (CRP-associated AS disease activity score) and BASMI (Ankylosing spondylitis metrology index) values were negatively correlated with vitamin D levels in 653 patients with axial spondyloarthropathy [36]. In a recently published meta-analysis, it was determined that high vitamin D levels may be inversely associated with AS activity and associated with a decreased risk of AS [37].

The relationship between OA and vitamin D was investigated by epidemiological studies, and various data were obtained. Bergink et al. [38] investigated the relationship between the development of radiographic knee OA and vitamin D levels in a 6.5-year follow-up and found that low vitamin D intake in the diet was associated with increased risk of radiographic knee OA progression. They emphasized that increasing vitamin D levels in the elderly, particularly in those with low bone density, can prevent worsening and development of knee OA. Similarly, in a systematic review, Cao et al. [39] showed strong evidence for an association between low levels of vitamin D and loss of cartilage in the knee joint. In our study, summer and winter vitamin D levels in the OA group did not differ from the control group. However, there was a difference between summer WOMAC mean value and winter WOMAC mean value, and vitamin D levels were significantly lower in winter. These results indicated a significant negative correlation between WOMAC values and vitamin D levels, and low vitamin D levels were associated with high pain scores in OA. However, there are some studies in contradiction to this data. Yazmalar et al. [33] found no significant relationship between seasonal vitamin D levels and WOMAC scores in OA patients. Arden et al. [40] did not find any significant difference in radiological progression and WOMAC pain, function, and fatigue scores of knee OA patients who underwent vitamin D supplementation and were followed up for 3 years, compared to the control group. Konstari et al. [41] showed that serum vitamin D levels were not associated with hip or knee OA incidence during a follow-up study of 805 healthy controls over a 22-year period.

Vitamin D deficiency has long been known to cause chronic fatigue and muscle aches. Vitamin D deficiency was shown to play a role in triggering especially sleep disturbances in FMS patients [42]. Heidari et al. [43] found that vitamin D deficiency is associated with nonspecific bone pain in female patients with chronic musculoskeletal pain (nonspecific skeletal pain, leg pain, back pain, joint pain and FMS). In our study, summer and winter vitamin D levels of FMS patients did not show any significant difference compared to the control group. This data lends support to the findings reported by De Rezende Pena et al. [44] that there was no significant difference between vitamin D levels of FMS patients and healthy controls and pain intensity was not associated with vitamin levels. In our study, winter FIQ value was higher than summer FIQ value in the FMS group, and the change was significant. In addition, winter D vitamin levels were significantly lower than summer values. Based on these values, a significant correlation was established between the seasonal variation of vitamin D and mean FIQ values. Wepner et al. [19] also found a significant decrease in FIQ questionnaire of FMS patients who underwent vitamin D replacement for 20 weeks. Okumuş et al. [45] reported that vitamin D levels of FMS patients showed a significant correlation with FIQ values, while low vitamin D levels affected pain and functional status. Conversely, Warner et al. [46] reported that 3 months of vitamin D replacement did not relieve pain in patients with chronic musculoskeletal pain.

In our study, mean HAD values in summer and winter were different, but the change was not significant. Mean HAD value did not differ significantly between summer and winter, while vitamin D levels were lower in winter. Therefore, there was no significant correlation between seasonal variation of vitamin D and mean HAD values. In contrast, in a study on FMS patients, Armstrong et al. [47] reported vitamin D deficiency in 13% of the patients, mild deficiency in 56% and normal vitamin D values for 30% and found higher HAD scores for the patients with deficiency, compared to other patients. In addition, Wepner et al. [19] reported that vitamin D replacement significantly reduced the HAD score.

Our study has several limitations. Some of these are the inadequate number of patients, that our groups are not homogeneous, that vitamin D is affected by many factors (disease stage, prognosis, existing treatment), that the level of 1,25 hydroxyvitamin D cannot be determined in our laboratory, that only specific parameters of disease activity were tested.

In conclusion, we think that it is necessary and important to determine vitamin D levels and provide supplementation to patients who need it in terms of contributing to the regulation of disease activity especially in patients with OA and FMS in physiatry practice. In order to determine the relationship between vitamin D and chronic diseases, there is a need for prospective studies with more patients.

Conflict of Interest

No conflict of interest was declared by the authors.

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Ethical approval

All participants were informed about the study and their consent in verbal and written form was obtained. Our study was approved by the hospital ethics committee (Approval no: 191). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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